

This listing of claims will replace all prior versions, and listings of claims in the application.

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- The chemical structure shows a macrocyclic compound with several stereocenters and substituents. The structure includes a central amide bond (N-Me) and a carbonyl group (C=O). Substituents include R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub>, Z, W, OY, and X. The stereochemistry is indicated by wedged and dashed bonds at various positions.

or a pharmaceutically acceptable salt thereof, wherein

R<sup>1</sup> and R<sup>2</sup> are independently H or C<sub>1-4</sub> alkyl, or R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline or homoproline residue;

R<sup>3</sup> is selected from the group consisting of a side chain of an amino acid and a first fluorophore;

$R^4$  is H or  $CH_3$ ;

R<sup>5</sup> is H, an amine protecting group, an amino acid residue, a polypeptide, a peptide which contains a second fluorophore, a chemical moiety bound to a solid support, or a moiety containing from about 1 to about 50 non-hydrogen atoms;

R<sup>6</sup> is an isoleucine side chain or a valine side chain;

W is O or NH;

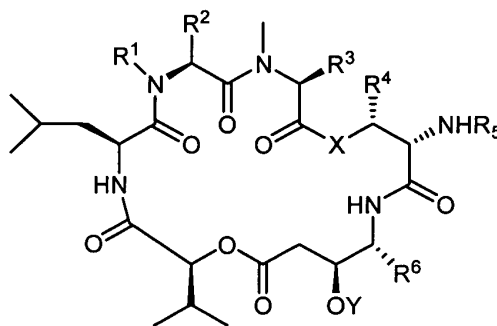
X is O or NH; and

Y is H or a hydroxyl protecting group;

Z is C(O) or C(O)-CH(CH<sub>3</sub>)-C(O);

provided that if R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, R<sup>4</sup> is methyl, and X is O, then R<sup>3</sup> is naphthylmethyl.

2. (Original) The compound according to claim 1 having the formula



or a pharmaceutically acceptable salt thereof, wherein

R<sup>1</sup> and R<sup>2</sup> are independently H or C<sub>1-4</sub> alkyl, or R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue;

R<sup>3</sup> is selected from the group consisting of a side chain of an amino acid and a first fluorophore;

R<sup>4</sup> is H or CH<sub>3</sub>;

R<sup>5</sup> is H, an amine protecting group, an amino acid residue, a polypeptide, a peptide which contains a second fluorophore, a chemical moiety bound to a solid support, or a moiety containing from about 1 to about 50 non-hydrogen atoms;

R<sup>6</sup> is an isoleucine side chain or a valine side chain;

X is O or NH; and

Y is H or a hydroxyl protecting group;

provided that if R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue, R<sup>4</sup> is methyl, and X is O, then R<sup>3</sup> is naphthylmethyl.

3. (Original) The compound according to claim 2, wherein R<sup>1</sup> is H and R<sup>2</sup> is methyl.
4. (Original) The compound according to claim 2, wherein R<sup>1</sup> and R<sup>2</sup> are methyl.
5. (Original) The compound according to claim 2, wherein R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue.
6. (Original) The compound according to claim 2, wherein R<sup>3</sup> is a side chain of an amino acid.
7. (Original) The compound according to claim 2, wherein R<sup>3</sup> is naphthylmethyl.
8. (Original) The compound according to claim 2, wherein R<sup>3</sup> is a benzyl group optionally substituted with OH, OCH<sub>3</sub>, CO(C<sub>6</sub>H<sub>5</sub>), F, Cl, Br, I, CH<sub>3</sub>, or C<sub>2</sub>H<sub>5</sub>.
9. (Original) The compound according to claim 2, wherein R<sup>3</sup> contains a fluorophore.
10. (Original) The compound according to claim 2, wherein R<sup>4</sup> is CH<sub>3</sub>.
11. (Original) The compound according to claim 2, wherein R<sup>4</sup> is H.
12. (Original) The compound according to claim 2, wherein R<sup>5</sup> is H.
13. (Original) The compound according to claim 2, wherein R<sup>5</sup> is an amine protecting group.
14. (Original) The compound according to claim 2, wherein R<sup>5</sup> is an amino acid residue or a polypeptide.
15. (Original) The compound according to claim 2, wherein R<sup>5</sup> contains a fluorophore.

16. (Original) The compound according to claim 2, wherein R<sup>5</sup> is selected from the group consisting of -(N-methyl)leucine;

- (N-methyl)leucine-proline;
- (N-CBz-N-methyl)leucine;
- (N-methyl)leucine-proline-lactate;
- (N-methyl)leucine-proline-pyruvate;
- (N-methyl)leucine-proline-lactate-glutamine-pyroglutamate;
- (N-methyl)leucine-proline-lactate-glutamine-cyclopentanoate;
- (N-methyl)leucine-proline-lactate-leucine-pyroglutamate;
- (N-methyl)leucine-proline-lactate-glutamine-cyclopentanoate;
- (N-methyl)leucine-proline-alanine-leucine-pyroglutamate, and
- (N-methyl)leucine-proline-(N-methyl)alanine-leucine-pyroglutamate.

17. (Original) The compound according to claim 2, wherein R<sup>6</sup> is a valine side chain.

18. (Original) The compound according to claim 2, wherein R<sup>6</sup> is a leucine side chain.

19. (Original) The compound according to claim 2, wherein Y is H.

20. (Original) The compound according to claim 2, wherein Y is a hydroxyl protecting group.

21. (Original) The compound according to claim 2, wherein X is O.

22. (Original) The compound according to claim 2, wherein X is NH.

23. (Original) The compound according to claim 2, wherein R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue; R<sup>3</sup> is a benzyl group optionally

substituted with one or more selected from the group consisting of OH, OCH<sub>3</sub>, CO(C<sub>6</sub>H<sub>5</sub>), F, Cl, Br, I, CH<sub>3</sub>, and C<sub>2</sub>H<sub>5</sub>; R<sup>4</sup> is H; R<sup>6</sup> is a valine side chain; X is O; and Y is H.

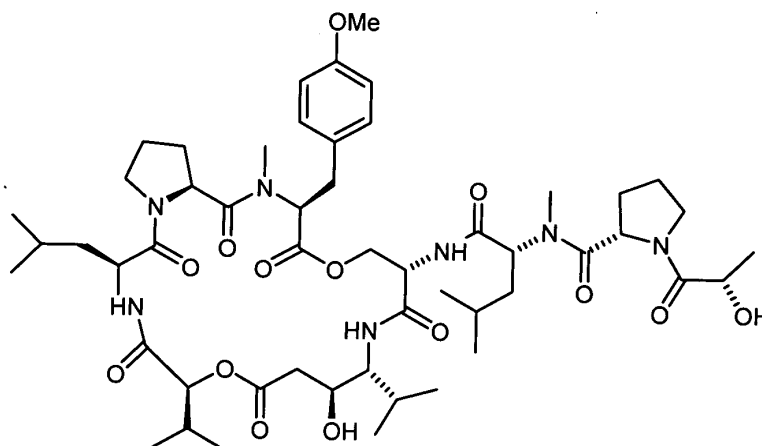
24. (Original) The compound according to claim 2, wherein R<sup>1</sup> is H; R<sup>2</sup> is CH<sub>3</sub>; R<sup>3</sup> is a benzyl group optionally substituted with one or more selected from the group consisting of OH, OCH<sub>3</sub>, CO(C<sub>6</sub>H<sub>5</sub>), F, Cl, Br, I, CH<sub>3</sub>, and C<sub>2</sub>H<sub>5</sub>; R<sup>4</sup> is CH<sub>3</sub>; R<sup>5</sup> is as defined above; R<sup>6</sup> is a valine side chain; X is O; and Y is H.

25. (Original) The compound according to claim 2, wherein R<sup>1</sup> is CH<sub>3</sub>; R<sup>2</sup> is CH<sub>3</sub>; R<sup>3</sup> is a benzyl group optionally substituted with one or more selected from the group consisting of OH, OCH<sub>3</sub>, CO(C<sub>6</sub>H<sub>5</sub>), F, Cl, Br, I, CH<sub>3</sub>, and C<sub>2</sub>H<sub>5</sub>, preferably OCH<sub>3</sub>; R<sup>4</sup> is CH<sub>3</sub>; R<sup>6</sup> is a valine side chain; X is O; and Y is H.

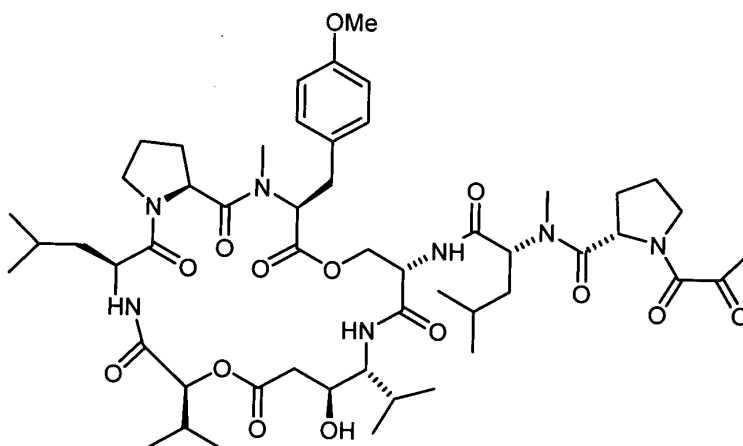
26. (Original) The compound according to claim 2, wherein R<sup>1</sup> and R<sup>2</sup> together form the alkyl ring of a proline residue; R<sup>3</sup> is a naphthylmethyl group; R<sup>4</sup> is CH<sub>3</sub>; R<sup>6</sup> is a valine side chain; X is O; and Y is H.

27. (Original) The compound according to claim 2, wherein R<sup>5</sup> consists of 1-5 amino acid residues.

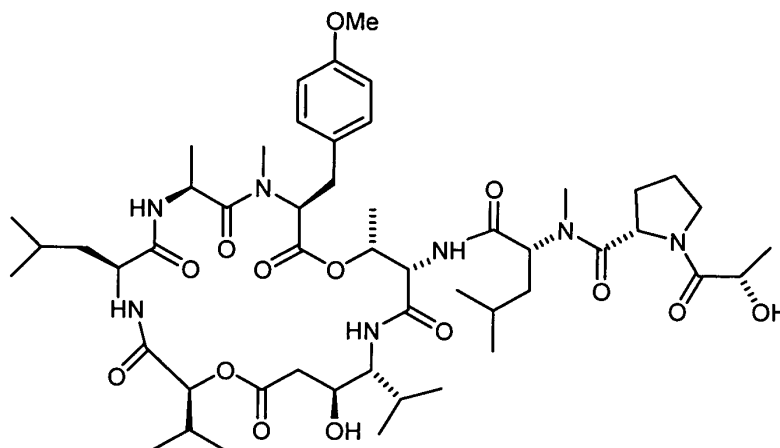
28. (Original) The compound according to claim 2, having the structure



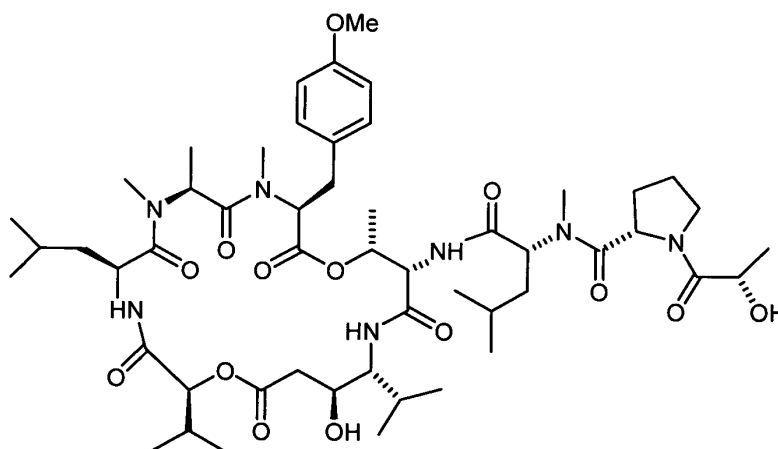
29. (Original) The compound according to claim 2, having the structure



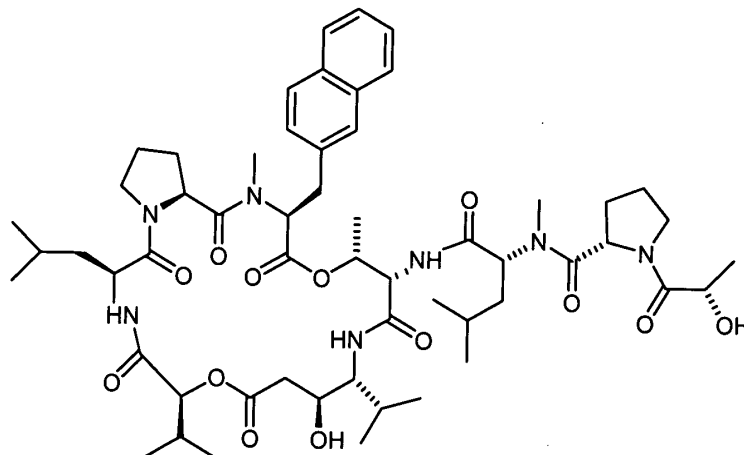
30. (Original) The compound according to claim 2, having the structure



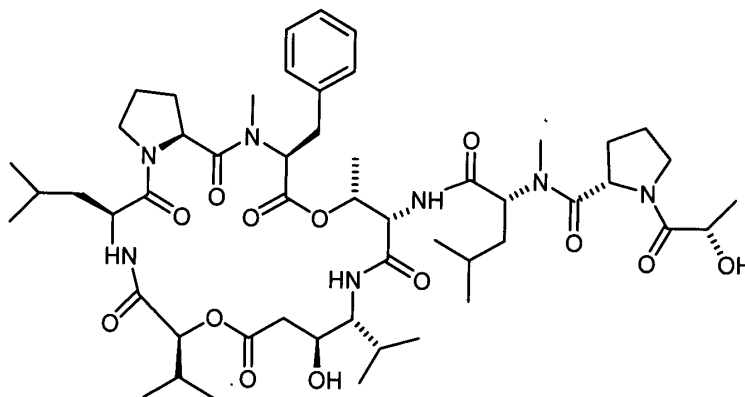
31. (Original) The compound according to claim 2, having the structure



32. (Original) The compound according to claim 2, having the structure



33. (Original) A compound having the structure



34. (Currently Amended) A composition comprising a compound according to claim 1 [[any of one of claims 1-33]] and a pharmaceutically compatible excipient or carrier.

35. (Currently Amended) A method of inhibiting, treating, or preventing tumorigenesis, comprising contacting a cell with an effective amount of a compound according to claim 1 [[any one of claims 1-33]].



36. (Currently Amended) A method of preventing or inhibiting the growth of a cancer cell, comprising contacting a cancer cell with an effective amount of a compound according to claim 1 [[any one of claims 1-33]].

37. (Currently Amended) A method of inhibiting or preventing protein synthesis, comprising contacting a cell or cellular component with an effective amount of a compound of claim 1 [[any one of claims 1-33]].

38. (Currently Amended) A method of enhancing apoptosis, comprising contacting a cell or cellular component with an effective amount of a compound according to claim 1 [[any one of claims 1-33]].

39. (Currently Amended) A method of providing immunosuppressive therapy, comprising administering to a subject in need thereof an effective amount of a compound according to claim 1 [[any one of claims 1-33]].